REPORT DOCUMENTATION PAGE

Form Approved

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
		Proceedings, 13 February 1995

4. TITLE AND SUBTITLE

Simulation of Oculomotor Post-Inhibitory Rebound Burst Firing Using a Hodgkin-Huxley Model of a Neuron

5. FUNDING NUMBERS

PE - 62202F
PR - 7755
TA - 27
WU - 15

6. AUTHOR(S)

John D. Enderle
Edward J. Engelken

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Armstrong Laboratory (AFMC)
Aerospace Medicine Directorate
Clinical Sciences Division, Flight Medicine Branch
2507 Kennedy Circle
Brooks AFB TX 78235-5117

8. PERFORMING ORGANIZATION

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

10. SPONSORING/MONITORING

AL/AO-PC-1995-0012

11. SUPPLEMENTARY NOTES

Armstrong Laboratory Technical Monitor: Dr. Edward J. Engelken, (210) 536-2715

12a. DISTRIBUTION/AVAILABILITY STATEMENT

Approved for public release; distribution is unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

A number of theories have been reported on post saccade phenomenon describing dynamic overshoot, glissadic overshoot and undershoot, and undershoot, all naturally and frequently occurring saccadic eye movements. Electrophysiological evidence for post-inhibitory rebound burst firing activity during saccadic eye movements is prevalent in the literature. However, the cause for the phenomenon is not known. Marked inhibition of neurons within the Paramedian Pontine Reticular Formation often results in post-inhibitory rebound burst firing activity at the beginning and end of a saccade. In this paper, post-inhibitory rebound burst firing activity after marked hyperpolarization is postulated to occur in the Paramedian Pontine Reticular Formation due to a low membrane threshold voltage. With this biophysical property, a single neuron is capable of firing at high rates automatically and without stimulation when released from inhibition. Simulations using the Hodgkin-Huxley model of a neuron demonstrate that a single neuron is capable of firing at high rates automatically without stimulation when released from inhibition.

14. SUBJECT TERMS	15. NUMBER OF PAGES
Saccade, Neural Network, Neuron, Fast Eye Movement, Neurosensory Control, Hodgkin-Huxley Model, Oculomotor System	6
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	UL

Simulation of Oculomotor Post-Inhibitory Rebound Burst Firing Using a Hodgkin-Huxley Model of a Neuron

John D. Enderle, Ph.D.
Electrical & Systems Engineering Dept.
University of Connecticut
260 Glenbrook Road, U-157
Storrs, CT 06269-3157

Edward J. Engelken, Ph.D.
Aerospace Medicine Directorate
Armstrong Laboratory/AOCF
Brooks AFB, TX 78235

KEYWORDS

Saccade, Neural Network, Neuron, Fast Eye Movement, Neurosensory Control, Hodgkin-Huxley Model, Oculomotor System

ABSTRACT

A number of theories have been reported on post saccade phenomenon describing dynamic overshoot, glissadic overshoot and undershoot, and undershoot, all naturally and frequently occurring saccadic eye movements. Electrophysiological evidence for post-inhibitory rebound burst firing activity during saccadic eye movements is prevalent in the literature. However, the cause for the phenomenon is not known. Marked inhibition of neurons within the Paramedian Pontine Reticular Formation often results in post-inhibitory rebound burst firing activity at the beginning and end of a saccade. In this paper, post-inhibitory rebound burst firing activity after marked hyperpolarization is postulated to occur in the Paramedian Pontine Reticular Formation due to a low membrane threshold voltage. With this biophysical property, a single neuron is capable of firing at high rates automatically and without stimulation when released from inhibition. Simulations using the Hodgkin-Huxley model of a neuron demonstrate that a single neuron is capable of firing at high rates automatically without stimulation when released from inhibition.

INTRODUCTION

Saccades are characterized by a rapid shift of gaze from one point of fixation to another, eye movements that are used in reading and quick scanning. Although the purpose for this type of movement is clear, that is to quickly move the eyeball to the target, the neural control strategy is not. Studies of the saccadic control mechanism have been based on the system identification technique and control systems [1]-[2], single-unit microelectrode recordings (for example, see [3]-[4]), muscle tension measurements, and general observations from the main sequence diagram [1]. In comparison with other systems, the oculomotor system is the best understood of all human control systems. However, significant and important differences still

exist regarding the control mechanism during saccadic eye movements. Physiological evidence indicates that saccades are controlled through a parallel distributed network involving the cortex, cerebellum, and brain stem. The saccadic neural activity of the superior colliculus and cerebellum, in particular have been identified as the saccade initiator and terminator, respectively, although neither is required for a saccade.

Enderle and coworkers have developed a new physiological neural network for saccade eye movement control [5]. Based on electrophysiological evidence, eye-movement measurements and systems control theory, a new local feedback model of horizontal saccadic neural control is described in [5]. The neural control mechanism is first order time optimal with pronounced stochastic rebound neural firing after marked inhibition. The neural circuit consists of neurons in the Paramedian Pontine Reticular Formation (PPRF), consisting of burst, tonic and pause cells, the vestibular nucleus, abducens nucleus, oculomotor nucleus, cerebellum, substantia nigra, nucleus reticularis tegmenti pontis, the thalamus, the deep layers of the superior colliculus and the oculomotor plant for each eye. The neural circuit is shown in Figure 2 of [5]. Agonist burst cell activity is initiated with maximal firing due to an error between the target and eye position, and continues until the internal eye position in the cerebellar vermis reaches the desired position, then decays to zero. The cerebellar vermis is also responsible for adapting the duration of maximal firing based on the initial position of the eye. Due to prior pause cell inhibition of the burst cells, stochastic rebound burst cell firing occurs, resulting in a temporary rise and fall firing above the maximal steady state burst firing level. Antagonist neural activity is inhibited during the agonist burst activity. After the agonist burst, antagonist neural activity rises with a stochastic rebound burst and from input from the fastigial nucleus, then falls to a tonic firing level necessary to keep the eye at its destination. The onset of the antagonist tonic firing is stochastic, weakly coordinated with the end of the agonist burst, and under cerebellar control.

To execute a saccade, a sequence of complex activities takes place within the brain, beginning from the detection of an error on the retina, to the actual movement of the eyes. A saccade is directly caused by a burst discharge from motoneurons in the agonist muscle and a pause in firing from motoneurons in the antagonist firing (pulse). During periods of fixation, the motoneurons fire at a rate necessary to keep the eye stable (step). The pulse-step discharge in the motoneurons is caused by discharges in the PPRF.

Qualitatively, a saccade occurs according to the following sequence of events within the PPRF. First, the ipsilateral Long Lead Burst Neurons (LLBN) are stimulated by the CNS neurons which initiate the saccade. The LLBN then inhibits the tonic firing of the Omnipause Neurons (OPN). When the OPN cease firing, the Medium Lead Burst Neurons (MLBN) are released from inhibition and begin firing. The ipsilateral Inhibitionary Burst Neurons (IBN) are stimulated by the ipsilateral LLBN and the contralateral fastigial nucleus of the cerebellum. The ipsilateral Excitatory Burst Neurons (EBN) are stimulated by the contralateral fastigial nucleus of the cerebellum, and when released from inhibition fire spontaneously. Except for

the fastigial nucleus, there are no other accepted excitatory inputs to the EBN. The spontaneous firing within the EBN is the subject of this report.

The burst firing in the ipsilateral IBN inhibit the contralateral EBN and abducens nucleus, and the ipsilateral oculomotor nucleus. The burst firing in the ipsilateral EBN cause the burst in the ipsilateral abducens nucleus, which stimulates the ipsilateral lateral rectus muscle and the contralateral oculomotor nucleus. With the stimulation of the ipsilateral lateral rectus muscle by the ipsilateral abducens nucleus and the inhibition of the ipsilateral medial rectus muscle via the oculomotor nucleus, a saccade occurs in the right eye. Simultaneously, with the contralateral medial rectus muscle is stimulated by the contralateral oculomotor nucleus and with the inhibition of the contralateral lateral rectus muscle via the abducens nucleus, a saccade occurs in the left eye. Thus the eyes move conjugately under the control of a single drive center. The saccade is terminated with the resumption of tonic firing in the OPN via the fastigial nucleus.

POST INHIBITORY REBOUND BURST FIRING

Electrophysiological evidence for post-inhibitory rebound burst firing activity during saccadic eye movements is prevalent in the literature. This behavior is described by large and maximal neural firing rates without any regard for the size of the eye movement or apparent stimulation. The cause for the phenomenon is not known. In this paper, post-inhibitory rebound burst firing activity after marked hyperpolarization is postulated to occur in the PPRF due to a low membrane threshold voltage within the axon hillock of the neuron. With this biophysical property, a single neuron is capable of firing at high rates automatically without stimulation when released from inhibition. According to the hypothesis of this paper, when released from inhibition, the EBN maximally fire automatically and without stimulation. Ipsilateral EBN are uninhibited at the start of the saccade, and contralateral EBN are uninhibited at the end of the saccade. We refer to this activity as a post inhibitory rebound bursting.

Support for post inhibitory rebound burst firing activity is derived from the reports by many investigators (see investigators in [5]). One investigator describes rebound burst responses from thalamic neurons after very marked hyperpolarizations. Other investigators report neurons within the thalamus that allow them to serve as single cell oscillators based on multi-threshold activity levels. Because the EBN have no known inputs besides the fastigial nucleus, the EBN are modeled as firing spontaneously when released from inhibition. This appears to be an essential property of the neuron, since EBN fire after release from inhibition even after the fastigial nucleus is lesioned.

HODGKIN-HUXLEY MODEL OF A NEURON

To investigate the effect of threshold voltage on the firing characteristics of a neuron, simulations are carried out using the nonlinear Hodgkin-Huxley model of neuron, which

describes the membrane potential at the axon hillock due to conductance changes [6]. The equation, parameterized for the giant squid axon, defines membrane potential V_o as a function of stimulus current I_m and active gate conductance for sodium and potassium, and is given by

$$-I_m = \bar{g}_K n^4 (E_K + V_o) + g_l (E_l + V_o) + \bar{g}_{na} m^3 h (E_{Na} + V_o) + C\frac{dV_o}{dt}$$

where

$$\frac{dn}{dt} = \alpha_n (1\text{-}n) - \beta_n n \qquad \frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h \qquad \alpha_n = 0.01 \times \frac{V + 10}{\exp\left(\frac{V + 10}{10}\right) - 1} \ \text{msec}^{-1}$$

$$\beta_n = 0.125 \exp\left(\frac{V}{80}\right) \ \text{msec}^{-1} \qquad \alpha_m = 0.1 \times \frac{V + 25}{\exp\left(\frac{V + 25}{10}\right) - 1} \ \text{msec}^{-1}$$

$$\beta_m = 4 \exp\left(\frac{V}{18}\right) \ \text{msec}^{-1} \qquad \alpha_h = 0.07 \exp\left(\frac{V}{20}\right) \ \text{msec}^{-1}$$

$$\beta_h = \frac{1}{\exp\left(\frac{V + 30}{10}\right) + 1} \ \text{msec}^{-1} \qquad V = V_o - |V_{r.p.}| \ \text{mv}$$

Each of the variables in this model are described in [6], and reflect the voltage and time dependence of sodium and potassium channels on the membrane potential. To investigate the effects of low threshold voltage, simulations using the Hodgkin-Huxley model of a neuron are carried out using TUTSIM , a continuous time simulator. Threshold voltage is defined as when the sodium current, i_{na}, characterized by the m and h differential equations, is greater than the potassium current, i_K, characterized by the n differential equation. Since sodium current changes more quickly and rapidly than the potassium current, changes in threshold voltage are accomplished via changing parameter values in the sodium equations. Sodium current has a rising component (the m equations) and a falling component (the h equations). Thus changes to threshold are easily carried out by changing the value of 25 to a lower value in the algebraic equation for α_m.

To illustrate how changing threshold voltage effects the firing rates of the neuron, three simulations are presented: a normal action potential stimulated by a current pulse of 17μA for 5.88 ms with no initial hyperpolarization as shown in Figure 1, a single burst firing of the neuron after coming out of marked hyperpolarization with the normal threshold voltage and without stimulation as shown in Figure 2, and automatic maximal burst firing of the neuron

after coming out of marked hyperpolarization with a low threshold voltage and without stimulation as shown in Figure 3.

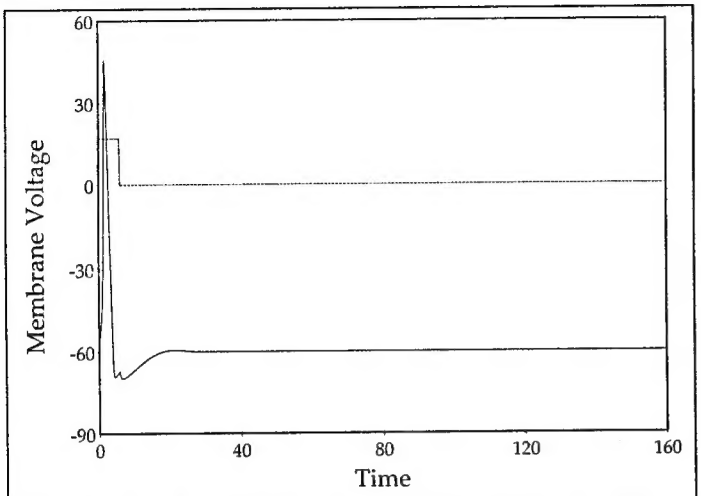

Figure 1. An action potential simulated with the Hodgkin-Huxley model. The current pulse is shown with dashed line and membrane potential is shown in solid line.

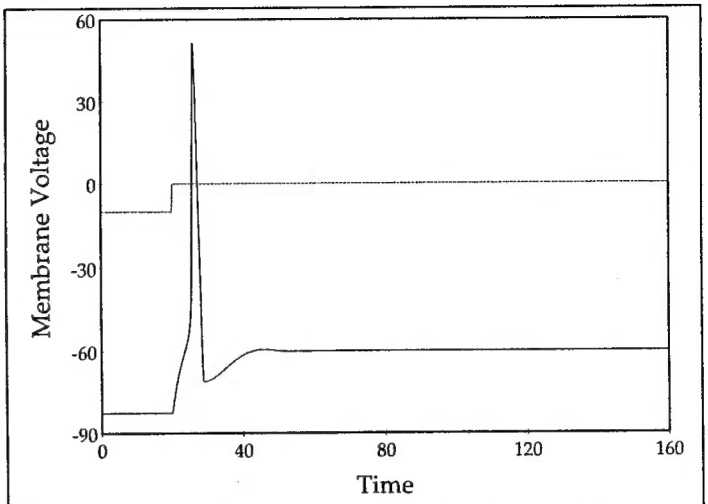

Figure 2. A -10 μA current pulse is used to hyperpolarize the cell membrane to - 80 mv for a very long time. After release from hyperpolarization at 20ms, a single action potential occurs, without any stimulation. The current causing hyperpolarization is shown with dashed line and membrane potential is shown in solid line.

DISCUSSION

The objective of this study was to investigate and postulate a mechanism based on biophysical phenomenon for post inhibitory rebound burst firing observed in EBN in the PPRF during saccades. This behavior is described by large and maximal neural firing rates without any regard for the size of the eye movement or apparent stimulation. Using a Hodgkin-Huxley model, simulation results support a post inhibitory rebound burst firing activity after marked hyperpolarization which is postulated to occur in the PPRF due to a low membrane threshold voltage within the axon hillock of the neuron. With this biophysical property, a single neuron is capable of firing at high rates automatically and without stimulation when released from inhibition. According to the hypothesis of this paper, the EBN has this property and when released from inhibition automatically and maximally fires without stimulation. The EBN are inhibited at all times except for the ipsilateral EBN which are uninhibited at the start of the saccade, and the contralateral EBN which are uninhibited at the end of the saccade.

Using the model of an EBN, which automatically and maximally fire without stimulation when released from inhibition, it is possible to explain many post saccade phenomenon, such as dynamic overshoot and glissades. Enderle and coworkers have shown it is possible to

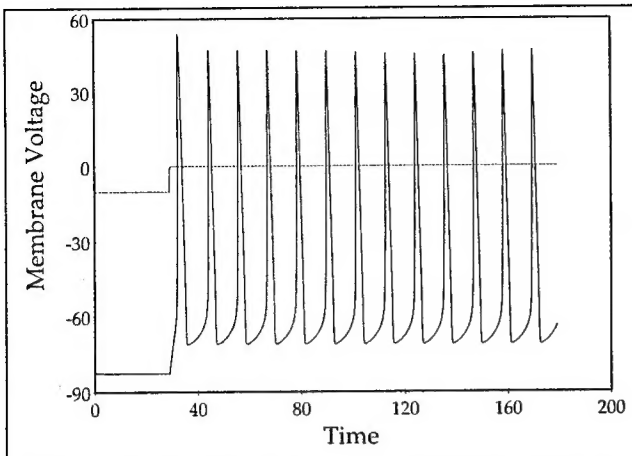

Figure 3. A -10 μA current pulse is used to hyperpolarize the cell membrane to - 80 mv for a very long time. Membrane threshold is changed from 25 to 10 to reflect the lower threshold voltage postulated for EBN. After release from hyperpolarization at 20ms, an automatic maximal frequency burst occurs without any stimulation. The current pulse is shown with dashed line and membrane potential is shown in solid line.

describe post saccade phenomenon with a common mechanism involving the firing activity in the contralateral EBN at the end of a saccade [5]. The work presented here further supports this mechanism by providing biophysics evidence.

Not considered in this paper is a more full and exact description of EBN firing activity. Note that the firing rates of these simulations are not characteristic of the EBN, which fire at much higher rates, but simply to show such a mechanism exists. Future work will involve modeling the EBN more exactly with a Hodgkin-Huxley model, including the potassium and sodium conductance channels, and also include potential dynamic changes in threshold voltage with time after marked hyperpolarization.

REFERENCES

1. Enderle, J.D., and Wolfe, J.W., Frequency response analysis of human saccadic eye movements: estimation of stochastic muscle forces. *Computers in Biology and Medicine*, 1988, 11(3): 195-219.

2. Enderle, J.D., and Wolfe, J.W., Time-optimal control of saccadic eye movements. *IEEE Transactions on Biomedical Engineering*, 1987, BME-34: 43-55.

3. Sparks, D.L., Translation of sensory signals into commands for control of saccadic eye movements: role of the primate superior colliculus. *Physiological Reviews*, 1986, 66: 118-171.

4. Noda, H., Cerebellar control of saccadic eye movements: its neural mechanisms and pathways. *Japanese Journal of Physiology*, 1991, vol. 41, no. 3, pp. 351-368.

5. Enderle, J.D., A Physiological Neural Network for Saccadic Eye Movement Control. Air Force Material Command, Armstrong Laboratory AL/AO-TR-1994-0023, 1994.

6. Hodgkin, A.L., Huxley, A.F., and Katz, B., Measurement of Current-Voltage Relations in the Membrane of the Giant Axon of *Loligo, Journal of Physiology*, 1952, 116: 424-448.